Remarks

Claims 1-16 are pending. Claims 4-6 and 11-16 as they read on methods of inhibiting paraptosis with the JNK inhibitor SP 600125 are under consideration in the instant application. Claims 1-3 and 7-10 have been withdrawn from consideration as being drawn to a non-elected inventions.

Rejections Under 35 U.S.C. §112, First Paragraph

The rejection of claims 4-6 and 11-16 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement allegedly because the specification provides no guidance as to how to inhibit paraptosis using SP600125 is respectfully traversed.

Base claim 4 is directed to a method of inhibiting paraptotic cell death in a cell by contacting the cell with an effective amount of the JNK inhibitor SP 600125, wherein the effective amount inhibits paraptotic cell death. Undue experimentation is allegedly required because a skilled artisan can only tell by experimentation whether paraptosis will occur and whether SP600125 inhibits such paraptosis.

Base claim 11 is directed to a method of treating a condition associated with excessive cell death by administering to a subject in need of such treatment an effective amount of the JNK inhibitor SP 600125, wherein the effective amount inhibits paraptotic cell death. Enablement is allegedly lacking due to the experimentation that would be required to determine the parameters for *in vivo* administration.

The specification teaches that inhibitors or neutralizing agents of the Jun N-terminal kinases (JNKs) JNK1 and JNK2, which are MAP kinases activated in response to cellular stress, block both the paraptotic and the apoptotic cell death pathways. The specification also teaches that the JNK inhibitor SP 600125 is a neutralizing agent useful in the taught methods of inhibiting paraptosis. Applicants further teach throughout the specification that neutralizing agents, defined as " agent effecting a decrease in the activity, amount or rate of expression of the prior art reference molecule or compound, for example, Jun N-terminal kinase 1 (JNK1) or JNK2" can be used to inhibit paraptosis. In addition, the specification exemplifies in Example II the inhibition of paraptosis in a human cell line with a neutralizing agent for JNK. In particular, Example II discloses that antisense oligonucleotide neutralizing agents for JNK1 or JNK2 were able to inhibit IGFIR-IC induced

paraptosis in 293T cells. An effective concentration of 50-100nM concentration for the neutralizing agents also is provided. Applicants submit that these teachings would provide the skilled artisan with sufficient guidance to develop any particular parameters related to particular embodiments without undue experimentation.

Applicants maintain that the fact that "further experimentation would be necessary" to determine particular parameters does not preclude enablement of the claimed invention as the Federal Circuit has made clear in *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342 (Fed. Cir. 1998):

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

152 F.3d at 1360.

In light of the above teachings and the well developed state of the art, Applicants contend that the application sufficiently enables those skilled in the art to practice the invention as claimed. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Regarding 35 U.S.C. §102

The rejection of claims 4-6 and 11-16 under 35 U.S.C. §102(e) as allegedly anticipated by Bennett et al. (U.S. Patent Application No. 2004/0072888) is respectfully traversed. The independent rejection of claims 4 and 5 under 35 U.S.C. §102(a) as allegedly anticipated by Bennett et al., *Procl. Nat. Acad. Sci. USA*, 98(24):13681-13686 (2001), also is traversed.

The filing date of Bennett et al. (U.S. Patent Application No. 2004/0072888) is March 24, 2003. The filing date of the above-identified application is February 19, 2002. Thus, Bennett et al. is not prior art to the instant application. If the Examiner wishes to rely on U.S. Serial No. 09/642 557, filed on Aug. 18, 2000, it is his burden to provide a copy of that application and show how each element of the instantly rejected claims is taught in U.S. Serial No. 09/642 557. Bennett et al.

is a continuation-in-part of U.S. Serial No. 09/642,557, such that it cannot be assumed that the teachings of the two specifications are identical.

With regard to claims 4 and 5, the Bennett et al. PNAS publication's mention of the term "apoptosis" allegedly anticipates the claimed invention. It is not Applicants' burden to prove that claim elements not taught by the Bennett et al. application are not necessarily present in the disclosures of Bennett et al. The Bennett et al. PNAS publication is silent about the SP 600125 induced inhibition of paraptosis in a cell. Apoptosis and paraptosis are distinct forms of cell death. The United States Patent and Trademark Office requires an examiner to supply an applicant either with a rationale for the inherent disclosure or evidence demonstrating the presence of the inherency and has long acknowledged that the initial burden in establishing an inherency rejection rests with the Examiner:

> in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristics necessarily flow from the teaching of the applied art.

Ex parte Levy, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

In view of the above, Applicants respectfully submit that Bennett et al. (U.S. Patent Application No. 2004/0072888) is not prior art to the instant application. With regard to claims 4 and 5, the Examiner has not met the burden of providing a basis in fact to reasonably support the determination that the allegedly inherent characteristics necessarily flow from the Bennett et al. PNAS publication. Accordingly, Applicants respectfully request removal of the separate rejections of claims 4-6 and 11-16 under 35 U.S.C. §102(e) as allegedly anticipated by Bennett et al. (U.S. Patent Application No. 2004/0072888) and claims 4 and 5 under 35 U.S.C. §102(a) as allegedly anticipated by Bennett et al., *Procl. Nat. Acad. Sci. USA*, 98(24):13681-13686 (2001).

Regarding 35 U.S.C. §103

The rejection of claims 6 and 11-16 under 35 U.S.C. §103(a) as allegedly rendered obvious by Bennett et al., *Procl. Nat. Acad. Sci. USA*, 98(24):13681-13686 (2001) as applied to claims 4 and 5 above, and in further view of Braun et al., *Expert. Opin. Investig. Drugs* 8(10):1599-1610 (1999) is respectfully traversed.

The deficiency of the primary reference, discussed in Applicants' rebuttal to the 102(a) rejection above, is not cured by the Braun et al. reference. As described Applicants' specification, paraptosis is distinct from apoptosis by the criteria of morphology, biochemistry and response to apoptosis inhibitors. For example, despite its lack of response to caspase inhibitors and Bcl-X_L, paraptotic cell death has been shown to be induced, among other inducers, by insulin-like growth factor I receptor (IGFIR) and mediated by an alternative caspase-9 activity that is Apaf-1 independent. Neither of the cited prior art references, viewed alone or in combination, teaches or suggests the claimed methods directed to inhibition of paraptosis. Accordingly, the combination of Bennett et al., *Procl. Nat. Acad. Sci. USA*, 98(24):13681-13686 (2001) and Braun et al., *Expert. Opin. Investig. Drugs* 8(10):1599-1610 (1999), cannot support the instant rejection under 35 U.S.C. §103(a). Accordingly, Applicants respectfully request removal of the rejection.

Conclusion

In light of the Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to contact the undersigned attorney with any questions related to this application.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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